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10/507,059	09/09/2004	Hoon Choi	O-2779	8288

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EXAMINER	
BERRIOS, JENNIFER A	

ART UNIT	PAPER NUMBER
1619	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/507,059	CHOI ET AL.	
	Examiner	Art Unit	
	Jennifer A. Berrios	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-11,20 and 27-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 9-11, 20 and 27-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the reply filed 5/4/2010, wherein claim 1 has been amended and claims 8, 12-19, 21-26 and 32-36 have been cancelled.

Currently claims 1-7, 9-11, 20 and 27-31 are being examined.

Maintained Rejections

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-7, 9-11, 20, 28-29 and 31 **remain** rejected under 35 U.S.C. 103(a) as being unpatentable over Shvets et al (Theoretical and Experimental Chemistry, Vol 37, No. 2, 2001, 112-115), Schacht et al (Science, Vol 273, 8/9/1996, 768-771, and Bellantone et al (US 6,482,444, filed 6/14/2000).

Regarding claims 1-4, 9-10, Shvets teaches characteristics of template formation in silica in acidic medium. Shvets teaches that the starting materials used were tetraethyl orthosilicate (TEOS) or tetrabutyl orthosilicate (TBOS), cetyltrimethylammonium bromide (CTMABr) or cetyltrimethylammonium chloride (CTMACl) and HCl to adjust the pH of the reaction medium. The composition was prepared as follows: CTMABr was dissolved in HCl and then the solution was transferred to a weighing bottle, TEOS or TBOS was added dropwise, the weighing bottle was closed and kept until the reaction was complete. Fibers first appeared after 5-12 days (depending on the room temperature). The reaction temperature affects particularly the rate of hydrolysis of the orthosilicate and correspondingly the rate of

growth of the fibers. Thus on increasing the temperature in the range of 10-24°C the induction time was reduced from 12 to 5 days and completion process from 30 to 10 days. At lower temperatures there was growth of fibers of greater diameter, greater length, and more order. It seems applicant is simple optimizing a well known process for forming silica fibers.

Although Shvets doesn't specifically teach the limitations of claims 1-4 and 9-10, since the process done by Shvets for the formation of fibers seems to be almost identical to the method of forming the fibers of the instant invention and all the same ingredients are utilized, as demonstrated by Example 1, it's expected that the properties of the fibrous preform of the instant application are also properties of the fibers created by Shvets.

It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Schacht teaches oil-water interface templating of mesoporous macroscale structures. Silica fibers are created dissolving C16H33N(CH3)3Br (synonymous to CTMABr) in HCl. To this solution TEOS is added slowly over 30 min. During this time an emulsion forms. Under slow forming, predominantly fiber-type morphologies are formed (768, col 3, par. 3; 769, col 1, par 1). With increasing stirring rate, more and more spherelike particles are formed until the fiber morphology disappears completely. The size of spherical particles decreases with increasing stirring rate. The particles are in fact hollow after the organic phase has been removed (Pg 769, par 3).

It would have been obvious to one of ordinary skill in the art to modify the process of Schacht, in order to create fiber or particles, as Schacht teaches that stirring rate can control the morphology of the fiber/particle created. Although Schacht teaches as a preferred embodiment creating particles, he does not discredit or teach away from using fibers.

These materials (i.e. the materials used to create sphere and/or fibers) have technological as well as fundamental implications. The hollow spheres, for instance, could be used for controlled drug delivery systems. The membranes might be developed further for separation processes, where nanometer-scale pores are needed (Pg 771, Par 1).

Shvets and Schacht fail to teach the fibrous composite to comprise biodegradable polymers, a bioactive agent or to be used to deliver a bioactive agent to an animal using a controlled release delivery system.

Regarding claims 1 and 5, Bellantone discloses a bioactive, biodegradable composite material comprising a fibrous composite of oxides and biodegradable polymers, such as polylactic/polyglycolic acid, wherein fibers of the porous composite comprise gel-like oxide materials with nanometer-sized pores (Col 6, lines 36 and 60-61; Col 7, lines 23-25; and Col 8, lines 23-25).

Regarding claims 2-3, the oxides comprise SiO2 and CIO and are bioactive and capable of inducing bone-like apatite growth (Col 2, lines 51-65; Col 3, lines 46-50).

Regarding claims 6-7, 28, and 31, Bellantone discloses the inclusion of a drug or a therapeutic composition to be delivered from the fibrous porous composite at a

controlled rate (Col 7, lines 49-57; Col 15, lines 64-66). The drug or therapeutic composition can comprise bone morphogenic proteins (Col 7, lines 62-63).

It would have been prima facie obvious to one of skill in the art at the time the invention was made to combine the teachings of Schacht, Bellantone and Shvet to arrive at the instant invention. One of skill in the art would have been motivated to substitute the silica fibers taught in Bellantone for the silica fibers taught by Shvet. One would have been motivated to do so because Schacht teaches that the materials used to create silica spheres can be used in controlled drug delivery systems. Since the starting materials of Shvet is similar to the starting materials of Schacht, it would be obvious to one of ordinary skill in the art that the silica fibers of Shvets would also be useful for use in controlled drug delivery systems. Schacht demonstrates that the materials used for creating silica spheres and/or fibers such as HCL, TEOS, CTMABr, have technical as well as fundamental implications and can be used in controlled drug-delivery systems. As such the resulting product from Shvets, created from the starting materials HCL, CTMABr and TBOS or TEOS, can also be used for controlled drug-delivery systems.

One of skill in the art would expect reasonable success because Shvet/Schachts and Bellantone teach fibrous composites of oxides useful for controlled release delivery systems.

Regarding claims 11, 20 and 29 it would have been obvious to one of skill in the art that in order to deliver the bioactive agent incorporated on the fibrous composite of claim 1, the composite must be administered to the patient in need.

With regard to the limitations of effecting release of the bioactive agent in an animal upon degradation of the fibrous porous composite, this is an expected property of the fibrous composite. Since Shvet/Schacht and Bellantone teach a fibrous porous composite similar to the fibrous composite of the instant invention, both comprising the same fibrous preform, bioactive agent and physical properties, it's expected that the composite taught by Shvet/Schachts/Bellatone would also have the same degradation properties as the composite taught by the instant invention.

Response to Arguments

Applicant argues that there are several significant differences between the materials taught by Shvets and/or Schacht and those of the present invention.

Applicant argues that the invention is specific to a fibrous preform comprising hollow core fibers. The claims do not include any claim to the method of synthesizing the composition. Instead, the claims are drawn to the composition itself, having hollow core fibers that upon formulation, self assemble into a preform construct. Also claimed are methods for using the construct to deliver a bioactive agent. Applicants' hollow core fiber preform was prepared as shown in FIG 1, and as described in paragraph [0077], wherein "After emulsification, terabutylorthosilicate (TBOS) as silicon source is added dropwise to the solution. The solution is held at room temperature for 5 to 7 days to allow reaction without stirring." This process results in a unique preform that can be shaped or cut to size ("sizable") for implant purposes ("wherein (i) nanopores ranging in size from 1.5 to 10 nm in diameter are on the surface of the interconnected fibers; and

wherein the resulting fibrous composite has an overall surface area of greater than 1000 m2/g; (ii) mesopores and macropores are interspaced between and among the interconnecting fibers of the porous configuration, and (iii) interfiber pore size ranges from 0.5 to 10 times fiber diameter"). It is inconceivable, if hollow core fibers had been produced in Shvets' formulation, that the authors would not have reported such a finding. While similar starting materials were used by Shvets, the preform assembly process was apparently different from Applicants', thereby producing different products.

This is not persuasive. Applicant claims that Shvets while having similar materials, is formed by a different process. Shvets teaches that CTMABr was dissolved in HCL and then the solution was transferred to a weighing bottle, TEOS or TBOS was added dropwise, the weighing bottle was closed and kept until the reaction was complete. Fibers first appeared after 5-12 days (depending on the room temperature). This process is almost identical to the process applicant has described above. While Shvets makes no mention of stirring, the Schacht is referred to teach that stirring rate can control the morphology of the fibers created.

Applicant further argues that the product produced by Shvets under the conditions used in that paper, is a population of solid fiber of various shapes - but which are nonporous and not hollow core - by Shvets' own description. This is not persuasive. Applicant has not demonstrated factual evidence demonstrating that the fibers of Shvets are all solid. Furthermore, Examiner can not find in the Shvets reference, where Shvets claims that all the fibers are solid. Applicant claims that by Shvet's own description describes fibers which are nonporous and not of hollow core. If seems applicant is

implying that all non-porous fibers, inherently do not have a hollow core. This is not persuasive, Examiner fiunds no definition if Shvets to support this conclusion. Furthermore, applicant has not provided factual evidence or support demonstrating that a nonporous fiber equals a solid fiber. A straw, for example, can be seen as a nonporous fiber, comprising a hollow core.

Applicant further states that Schacht's hollow spheres may aggregate into fibers and steps are taken to avoid such aggregates. This is not found persuasive as Schacht says that the sphere aggregate into lumps and steps can be taken to avoid such aggregates. Nowhere does Schacht define the aggregates as fiber aggregates and steps can be taken if wanted, as such it's optional, not mandatory. The Schacht reference also does not teach that the hollow fibers cannot be made or used, and/or it doesn't discourage one of skill in the art from making and/or using hollow fibers.

Applicant argues even if Bellantone were added to the combined Shvets and Schacht references, the resulting composition would still be one of hollow spheres. However, the difference between hollow spheres and hollow core fibers is not simply nomenclature.

This is not persuasive, as stated in the rejection, Schacht teaches that the morphology of the fiber/particles can be controlled by controlling the stirring rate of the solution, as such one of skill in the art would be motivated to optimize the quantity of stirring in order to achieve an ideal fiber or particle morphology.

Applicant further argues that the combined prior art offers no teaching or suggestion for how to obtain or form hollow core fibers, let alone how to produce hollow-

core fibers having the useful, ductile, and easily handled characteristics of Applicants' invention. This is not persuasive, applicant is arguing limitations not recited by the instant claims.

Applicant further argues that their methods does not use an organic solvent in the formation of an oil phase. By comparison, in the cited combined prior art precursors, such as TEOS, was dissolved in an organic solvent (for example, mesitylene, see first paragraph ofp. 769 of Schacht et al.) to constitute an oil phase, which then reacts with the water phase to obtain the final product. In contrast, in Applicants' method, TBOS forms the oil phase itself and no other organic solvent was added (self-assembling into a "fibrous preform").

This is not persuasive, it is noted that the Shvets reference is used to teach a similar method of making and not the Schachts reference, which is simply relied upon to teach the relationship between stirring rate and morphology and the connection between hollow particles/fibers for use in controlled release devices. The Shvets reference does not disclose the use of an organic solvent and further disclosed that the composition of the reaction mixture comprises, HCL, CTMABr, TEOS or TBOS and water, thus no organic solvents.

In response to applicant's arguments against the Bellantone reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231

USPQ 375 (Fed. Cir. 1986). Bellantone need not teach all the limitations of claims rejected, as the cited combined reference do teach all the limitations.

7. Claims 27 and 30 **remain** rejected under 35 U.S.C. 103(a) as being unpatentable over Shvets et al (Theoretical and Experimental Chemistry, Vol 37, No. 2, 2001, 112-115), Schacht et al (Science, Vol 273, 8/9/1996, 768-771, and Bellantone et al (US 6,482,444, filed 6/14/2000) as applied to claim1-7, 9-11, 20, 28-29 above, and further in view of Aloha et al (WO 97/45367).

Shvets/Schacht/Bellantone teach all the limitations of claims 20 and 11, upon which claims 27 and 30 depend on, but fail to teach the limitations further recited by claims 27 and 30.

With respect to claims 1 and 5, Ahola et al. discloses a bioactive, biodegradable composite material comprising a fibrous composite of oxides and biodegradable polymers (polylactic acid), wherein fibers of the fibrous composite comprise gel-like oxide materials with nanometer-sized pores (pg. 5, lines 19-27; pg. 10, lines 1-10, 18-25; pg. 13, line 27 – pg. 14, line 1; pg. 14, lines 16-18).

With respect to claims 6 and 11, Ahola et al. discloses the inclusion of a drug or therapeutic composition to be delivered at a controlled rate from the fibrous composite (col. 4, lines 29-32; col. 10, lines 12-14, 26-30).

With respect to claim 7, Ahola et al. discloses the therapeutic composition comprises bone morphogenic protein (pg. 6, lines 10-11, 34-36).

With respect to claims 20 and 21, Ahola et al. discloses the drug or therapeutic composition is administered to an animal (human or animal body) at a site needed (pg. 4, line 10-12, 32 - pg. 5, line 5).

It would have been prima facie obvious to one of skill in the art at the time the invention was made to combine the teaching of Shvet/Schacht/Bellantone and Aloha to arrive at the instant invention. One of skill in the art would have been motivated to administer the fibrous composite taught by Shvet/Schacht/Bellantone to a human, as suggested by Aloha. One in the art would expect reasonable success because both Aloha and Shvet/Schacht/Bellantone teach fibrous composites of oxides and biodegradable polymers, comprising bioactive agents (bone morphogenic proteins) to be released at a controlled rate.

Response to Arguments

Applicant argues that the Ahola reference required "post-formulation assembly" and therefore cannot by definition be "self assembled." As such it cannot render the applicant independent claim 1 obvious.

This is not found persuasive as Ahola is simply referenced to provide motivation to deliver the bioactive agent to a human, using a fibrous composite. Ahola need not teach all the limitations of claims rejected as the cited combined reference do teach all the limitations.

Applicant further asks why Examiner states that Svets/Schachts/Bellantone teach all of the limitations of claims 20 and 11 upon which claims 27 and 30 depend, but fail to

teach the limitations further recited by claims 27 and 30. How is this possible? Claims 27 and 30 narrow the invention, they do not broaden it.

Examiner would like to note that the above statement, is simply means that Svets/Schachts/Bellantone teach all the limitations of claim 20 and 11, the broader claims, but do not teach the fibrous composite to be delivered to a human, the limitation "to a human," being the limitations further recited by instant claims 27 and 30.

Conclusion

8. No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer A. Berrios whose telephone number is

(571)270-7679. The examiner can normally be reached on Monday-Thursday: 7:00am-4:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 270-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer A Berríos/
Examiner, Art Unit 1619

/Tracy Vivlemore/
Primary Examiner, Art Unit 1635